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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,616	05/04/2001	Peter Sebbel	1700.0180002/JAG/BJD	6018

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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	14

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/848,616	SEBBEL ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *5/9/2002, 8/7/2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☐ Claim(s) *1-27,32,33,39,40,45-47,57-60,63-77,81,82 and 86-110* is/are pending in the application.

4a) Of the above claim(s) *1-27,32,33,39,40,45-47,57-60,63-77,81 and 82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *86-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Newly filed claims 87-89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 9. Claims 90-110 have been examined only to the extent that they read upon the elected species, 90% identity to SEQ ID NO: 158. Note, SEQ ID NO: 134 differs from SEQ ID NO: 158 by more than just a substitution at amino acids 79 and 80; a quick visual inspection indicates additional differences at e.g. positions 35 and 40. In any case, 90% identical to SEQ ID NO: 134 or 90% identical to residues 1-149 of SEQ 134 is not the same as 90% identical to SEQ 158, even if there is some overlapping subject matter.

Claim Rejections - 35 USC § 103

Claims 86, 90-94, 96-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett 6,231,864 in view of Mark et al 4,959,314 and Zhou et al (Journal of Virology 66(9): 5393-5398, 1992), for reasons similar to the previous rejection applied to claims 36 and 38.

As discussed in the previous Office action, Birkett teaches hepatitis B core particles modified to contain a chemically reactive amino acid (such as lysine inserted at residue 78), and chemical conjugation of an antigenic determinant to the reactive amino acid by a linker. Birkett's core sequence is more than 90% identical to SEQ ID NO: 158. Birkett differs from the claimed invention only in that Birkett does not teach modification of the cysteine residues corresponding to positions 48 and 110 in SEQ ID NO: 158. However, as discussed previously, Mark teaches deletion or replacement of nonessential cysteines to reduce or eliminate undesirable intramolecular or intermolecular cross linking, and Zhou teaches that all of the HBV core cysteines are nonessential for assembly of core particles. Therefore, it would have been obvious to delete or replace some or all of the HBV core cysteines, including these two, to achieve the

advantages taught by Mark, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 95 is rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett in view of Mark et al and Zhou et al as applied to claims 86, 90-94, 96-107 above, and further in view of Neurath et al 5,565,548. As discussed in the previous rejection of claims 43 and 78, this claim further limits the invention by requiring that the attached immunogenic determinant induce an immune response against an allergen. Birkett teaches that any hapten against which antibody production is desired can be attached to the modified HBV core particle, see column 13, lines 37-40. Birkett does not specifically discuss antibody production against allergens. However, Neurath teaches combination of HBV and allergen immunogens see for example the Abstract and claims 1-2. Therefore, an immunogenic determinant of an allergen would have been an obvious species to choose within the broad teachings of Birkett. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 108-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett in view of Mark et al and Zhou et al as applied to claims 86, 90-94, 96-107 above, and further in view of Davis et al WO 98/40100. As discussed in the previous rejection of claims 83-85, these claims further limit the invention in that they specify inducing a Th2 response, without generating a Th1 response. As discussed above, Birkett suggests combination of modified HBV core particles with adjuvants. One of the suggested adjuvants is alum, see column 24, line 1; alum is well known to be commonly used in human vaccines. Davis et al teaches that the combination of alum with hepatitis B particles leads to a Th2 response, without Th1 response, see page 25. Therefore, for one of ordinary skill in the art wishing to induce a TH2 response, it would have been obvious to choose the alum-adjuvanted embodiment suggested by Birkett, with reasonable expectation of success.

Response to Arguments

Applicant argues that Birkett does not teach the cysteine modifications, and asserts that Mark and Zhou do not cure the deficiency because they do not teach or suggest core particles having the amino acid sequence characteristics recited in the claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Mark provides reasons to modify nonessential cysteines, Zhou teaches that any and all of the cysteines are nonessential in the HBV particle, and the combined teachings of the references suggest modification of the cysteines (including the recited cysteines) in the particle of Birkett. Applicant has not pointed to any unexpected result, therefore it is maintained that the invention as claimed is prima facie obvious.

Double Patenting

Claims 86, 90-110 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim100-114 of copending Application No. 10/050,902. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims include the array based upon the cysteine-modified derivative of SEQ ID NO: 158.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 86, 90-110 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-16 of copending Application No. 10/050,898. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims include the array based upon the cysteine-modified derivative of SEQ ID NO: 158.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 703-308-2926. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800 /1600

10/30/03